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09/121,849	07/24/1998	ROBERT E. GARFIELD	SCH1237DI	3757

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EXAMINER

LILLING, HERBERT J

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 06/18/2002

27

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. 27

Application Number: 09/121,849
Filing Date: July 24, 1998
Appellant(s): GARFIELD ET AL.

Attorney Nancy J. Axelrod
For Appellant

EXAMINER'S ANSWER

MAILED
JUN 18 2002
GROUP 2900

This is in response to the appeal brief filed March 13, 2002.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

No amendment after final has been filed.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct

Art Unit: 1651

(7) Grouping of Claims

The rejection of claims 14, 17-19 and 20 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,508,045

HARRISON ET AL.

2-1994

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14, 17-19 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al U.S. 5, 508,045 obtains benefit of the earlier filing date for the subject matter relied upon for the rejection.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Harrison et al., teaches in column 1, lines 14-23:

"This invention concerns a method and agents for control, management and inhibition of a preterm labor or for inducing labor in overterm pregnancy by providing to a pregnant woman or pregnant mammal a donor or inhibitor of nitric oxide alone or in combination with other enhancing or modulating agents. In particular, this invention concerns a method for management and inhibition of preterm labor by administering to a pregnant woman a nitric oxide source in a safe and non-toxic concentration during the preterm labor or a nitric oxide inhibitor during the overterm pregnancy."

and

in column 2, lines 4-13:

"Once preterm labor is diagnosed, the risks and benefits of labor inhibition must be weighed against those of allowing delivery to occur. The risks from labor inhibition are primarily related to the side effects of the labor inhibiting drugs. Once preterm labor is diagnosed and the gestational age is established as appropriate for labor inhibition, contraindications such as eclampsia, preeclampsia, ruptured placenta, dead or anomalous fetus, fetal distress or chorioamnionitis to premature delivery is determined and the particular available tocolytic agent is selected."

which disclosure is clearly within the intended use for the claimed composition per se as recited:

Art Unit: 1651

..... "in amounts effective to ameliorate the symptoms of preeclampsia accompanied or unaccompanied by preterm labor in a pregnant female mammal, dysmenorrhea, or functional uterine bleeding or hemorrhaging."

The prior art reference to Harrison et al clearly teaches each of the three required components in the claimed compositions comprising (a) nitric oxide donor, (b) progestin and (c) a cyclooxygenase inhibitor as noted in the following disclosure of Harrison et al:

(b) nitric oxide donor which includes those of claimed in Claim 17 which recites:

"..... the nitric oxide donor is sodium nitroprusside, nitroglycerin, glyceryltrinitrate, SIN-1, isosorbidmononitrate or isosorbiddinitrate."

See column 20, line 60 through column 21, line 9:

"Nitric oxide source" means nitric oxide donor or precursor capable of potentiating the effect, or increasing the level of nitric oxide in utero and include but are not limited to S-nitroso-N-acetylpenicillamine (SNAP) and analogues thereof, nitric oxide nucleophiles or nitric oxide adducts such as diethylamino/nitric oxide (DEA/NO), DETA/NO or spermine or other nucleophilic groups known in the art, **nitroglycerin** and analogues thereof such as **isosorbide dinitrate**, nitropaste, nitropatches, **nitroprusside** and analogues thereof, ..."

(a) requires a progestin which is clearly indicated as one of the tocolytic agents by the reference, see column 20 under

" VI. Pharmaceutical Compositions "

"a. Compositions for use in Method I

This invention provides compositions suitable for control, inhibition and management of preterm labor.

The composition typically comprises a uterine relaxant selected from the group consisting of agents capable of potentiating the effect, or increasing the level, of nitric oxide in utero, such as nitric oxide donors, substrates, precursors and sources, and mixtures thereof.

Art Unit: 1651

Optionally, a second agent selected from the group consisting of other tocolytic agents, analgesics, vasopressors, and mixtures thereof are added to the nitric oxide source."

See column 22, lines 12-20:

"The **progestins** provided for use as tocolytic agents include **progesterone**, pregnanolone, pregnanediolone, epipregnanolone, allopregnanolone, allopregnanediolone, analogues thereof, and other agents known in the art. The progestins may be present in the composition in an amount of about 0.5 to 30 wt %, and more preferably 1 to 15 wt %. However, other amounts are suitable. The ethanol may be present in an amount of about 1 to 20 wt %, and more preferably about 5 to 15 wt %. However, other amounts are also suitable."

And the final component:

(c) a cyclooxygenase inhibitor ...which is disclosed in the reference in column 21, lines 26-35 and 54-62:

"Other tocolytic agents suitable for use in the labor retarding composition as the second agent include .beta.-adrenergic agonists, oxytocin antagonists, prostaglandin synthesis inhibitors such as prostaglandin synthetase inhibitors, magnesium salts, calcium transport blockers, ethanol, phosphodiesterase inhibitors, and progestins, among others.

Typically, the other tocolytic agents may be present in the composition in an amount of about 0.01 to 90 wt %, and more preferably about 1 to 25 wt %. However, other amounts may also be utilized."

"Prostaglandin synthesis inhibitors suitable for use as tocolytic agents include indomethacin (1-(p-chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic acid), naproxen, aspirin, meclofenamic acid, phenylbutazone, analogues thereof, and other agents. The prostaglandin synthesis inhibitors may be present in the composition in an amount of about 0.01 to 90 wt %, and more preferably about 1 to 10 wt %. However, other amounts are also suitable"

It is also noted that "aspirin" may be employed in the compositions as an analgesic as taught in column 22, lines 32-45:

Art Unit: 1651

"The present composition may also include other agents typically used for administration to a preterm labor patient. Some of these agents such as, for instance, those intended for countering the side effects of the components of the composition, are listed below. However, other agents may also be incorporated in amounts that are known to the practitioner.

Analgesics for use in conjunction with the present nitric oxide source include acetaminophen, acetylsalicylic acid [aspirin], morphine, fentanyl, or other similar acting agents known in the art, and mixtures thereof. The analgesics may be present in the composition of the invention in an amount of about 0.1 to 18 wt %, and more preferably about 5 to 20 wt %. However, other amounts are also suitable."

In accordance with *Graham v. John Deere Co* decision, the scope and contents of the prior art clearly teaches that the prior art teaches the components of the claimed pharmaceutical compositions employed for the same methods for treating *a female mammal*.

The reference does not specifically teach the combination of the claimed three components in a single composition.

It is considered the compositions are prima facie obvious to one that one of ordinary skilled in the art having the reference before him/her since the prior art would have motivated one to employ any combination of the claimed "mixture" as noted above since the agents are functionally equivalent behaving in the same manner to treat the same symptoms:

"Optionally, a second agent selected from the group consisting of other tocolytic agents, analgesics, vasopressors, and mixtures thereof are added to the nitric oxide source."

This disclosure is clear that one would be **motivated to employ mixtures** which includes any of the **functionally equivalent agents** which includes "progestin" and "a cyclooxygenase inhibitor" which aspirin is well known in the art to one of ordinary skilled in the art. It would have been obvious that one of ordinary skilled in the art would have reasonably expectation of success that any combination of agents, which includes the combination of nitric oxide donor with the two additional tocolytic agents of progestin and aspirin, would be within the scope of the prior art invention for controlling and managing the same symptoms as claimed, thus rendering the claimed pharmaceutical composition unpatentable over the prior art.

The specification does not disclose unexpected results commensurate in scope with the broad claimed inventions to overcome the prima facie case of obviousness over the reference of record.

(11) Response to Argument

Essentially the only response to the rejection is:

"Harrison discloses a laundry list of optional agents that can be present, in addition to applicants' component (b), in its composition."

"Thus, it is clear that Harrison suggests very generically an infinite set of possible combinations. Such a broad statement does not render obvious any particularly subsumed combination of specific compounds, which may happen to satisfy the recitations of the claims here. Without more, there can be no motivation to make the selections leading to the claimed invention. See, *In re Baird*, 29 USPQ2d 1550 (Fed. Cir. 1994)."

In accordance with the M.P.E.P.4141.01, the following considerations must be applied for Examiners to make obviousness rejections.

A. The claimed invention must be considered as a whole; --the reference is considered to be analogous prior art, which employs functionally equivalent agents for treating same symptoms as claimed.

B. The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination. This condition is clearly taught by the reference that teaches **functionally equivalent agents and mixtures** of the tocolytic agents with the nitric oxide donor which pharmaceutical compositions would be reasonably expectation of success to behave in the same manner to control and manage the symptoms which renders the claims obvious.

C. The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention. The single reference, Harrison et al., teaches each of the components even if as applicant argues "a laundry list" one would be motivated to select the three agents since one of ordinary skilled in the art would have expected each and every one of the components to be functionally equivalent to behave in the same manner within the disclosed ranges with a reasonably high degree of expectation of success in controlling the symptoms.

D. Reasonable expectation of success is the standard with which obviousness is determined. Appellant has argued:

"Thus, Harrison discloses three different categories of agents that can be used in addition to an NO donor; each of these categories is essentially infinite in scope. Harrison provides no general guidance (motivation) to select the particular (a) and (c) for combinations with (b) as recited in the instant claims from the myriad of compounds disclosed in Harrison. Absent such guidance, the reference does not render the claimed invention obvious."

There are several examples demonstrating various combinations of nitric oxide precursors or donors with various other agents that demonstrated success which agents are considered to be functionally equivalent. Applicant has not demonstrated any showings to rebut the prima facie case of obviousness over the reference of record. The reference teaches that the functionally equivalent agents would behave with a reasonable expectation of success absent a showing to the contrary that one or more of the agents would behave in a different manner. Thus, one would be highly motivated to employ the claimed (a) and (c) with (b) the nitric oxide donor in accordance with the teachings of the Harrison et al reference to employ mixtures which renders the claimed compositions prima facie obvious in view of the reference since the guidance for the selection of functionally equivalent agents employed as mixtures is stated by the reference (see column 20, lines 49-59) and as noted in the above paragraphs.

Appellants have indicated support for their positions are drawn to the decision, *In re Baird*, 29 USPQ2d 1550 (Fed. Cir 1994) on page 4 last line and page 5, end of third and fourth paragraph, which fact situation is totally different from the issues presented in the selection of agents in the Harrison et al reference. A copy of the *In re Baird* decision attached for the Board, which decision indicated that the selection process involved a selection of one specific diphenol compound from a generic claim that contained a large

number of variables which encompassed an estimated 100 million different diphenols. The conclusion by the Appeals Court was the specific compound was not even recited and there was no suggestion for the specific diphenol in the patent reference and "thus does not motivate its selection.". The fact situation is totally different since there is an exceptionally limited number of specific agents and there is a motivation for the selection of the specific agents.

Appellants have also indicated on page 6 a decision to *In re Vaeck 20 USPQ 1438 (Fed Cir. 1991)* to support the following argument which recites:

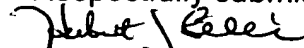
"Neither Harrison nor what was known to one of skill in the art would have provided motivation to modify Harrison's composition to arrive at applicants' claimed composition. That is, there was no motivation to achieve a composition which includes, in addition to compound (b) both compounds (a) and (c). Absent such motivation, with the requisite reasonable expectation of success, the reference does not render obvious the claimed invention. *In re Vaeck 20 USPQ 1438 (Fed Cir. 1991).*"

A copy of the decision is attached for the Board. This decision is not drawn to the same fact situation in view of the fact that the obviousness rejection was based on a substitution of one bacterial substance for another bacterial substance. It was determined by the Appeals Court that there was a substantial difference between the two bacterial substances. In addition, the substitution included a combination of art to make the substitution to make the obviousness type rejection which rejection was found to be defective since the substances were not functionally equivalent, thus the fact situation is again totally different from the issues in the appealed claims.

Art Unit: 1651

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,



HERBERT J LILLING

Primary Examiner

Art Unit 1651

May 22, 2002

Conferees

SPE Michael Wityshyn

SPE Gary Jones

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Supervisory Patent Examiner

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W. Gary Jones

Supervisory Patent Examiner

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Conferee

FULL TEXT OF CASES (USPQ2D)

All Other Cases

In re Baird (CA FC) 29 USPQ2d 1550 (1/19/1994)

In re Baird (CA FC) 29 USPQ2d 1550

In re Baird

U.S. Court of Appeals Federal Circuit
29 USPQ2d 1550

Decided January 19, 1994

No. 93-1262

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions _
(§ 115.0903.03)

Application claim for flash fusible toner is not obvious in view of prior patent, even though generic diphenol formula of patent encompasses bisphenol A of claim, since disclosure of generic formula that may encompass claimed compound does not, without more, render compound obvious, and since generic diphenol formula of patent contains large number of variables and encompasses estimated 100 million different diphenols in addition to bisphenol, but patent does not suggest selection of specific variables to formulate that compound and specifically discloses diphenols which are different from, and more complex than, bisphenol A; prior patent's specific enumeration of derivatives of bisphenol A does not warrant contrary conclusion, since suggestion of certain complex bisphenol A derivatives does not describe or suggest bisphenol A itself and thus does not motivate its selection.

Case History and Disposition:

Page 1550

Appeal from the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences.

Patent application of Brian W. Baird, Art F. Diaz, William H. Dickstein and Charles M. Seymour, serial no. 07/333,524 (flash fusible toner resins). From decision upholding examiner's final rejection of claims 1-5 on ground of obviousness under 35 USC 103, applicants appeal. Reversed.

Attorneys:

John A. Brady, Lexington, Ky., for appellant.

Adriene B. Lepiane, assistant solicitor, PTO (Fred E. McKelvey, solicitor, and Richard E. Schafer, associate solicitor, with her on brief), for appellee.

Judge:

Before Michel, Plager, and Lourie, circuit judges.

Opinion Text

Opinion By:

Lourie, J.

Applicants Brian W. Baird, Art F. Diaz, William H. Dickstein, and Charles M. Seymour (collectively Baird) 1 appeal from the October 15, 1992 decision of the U.S. Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences, Appeal No. 92-0860, affirming the examiner's final rejection of claims 1-5 of application Serial No. 07/333,524, entitled "Flash Fusible Toner Resins," as unpatentable on the ground of obviousness under 35 U.S.C. Section 103 (1988). We reverse.

Page 1551

BACKGROUND

Baird's application is directed to a flash fusible toner comprising a polyester of bisphenol A and an aliphatic dicarboxylic acid. Synthesis of the toner compositions involves the acetylation of bisphenol A and the reaction of that product with an aliphatic dicarboxylic acid selected from the group consisting of succinic acid, glutaric acid, and adipic acid. The application discloses that toners containing bisphenol A have optimal characteristics for flash fusing including, *inter alia*, high thermal stability and low critical surface energy.

Claim 1, the only claim at issue, reads as follows:

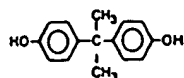
1. A flash fusible toner comprising a binder resin which is a bisphenol A polyester containing an aliphatic di [carboxylic] acid selected from the group consisting of succinic acid, glutaric acid and adipic acid.

Claim 1 stands rejected as obvious over U.S. Patent 4,634,649 to Knapp et al., which relates to developer compositions comprised of, *inter alia*, the polymeric esterification product of a dicarboxylic acid and a diphenol of the following generic formula:



wherein R is selected from substituted and unsubstituted alkylene radicals having from about 2 to about 12 carbon atoms, alkylidene radicals having from 1 to 12 carbon atoms and cycloalkylidene radicals having from 3 to 12 carbon atoms; R' and R'' are selected from substituted and unsubstituted alkylene radicals having from 2 to 12 carbon atoms, alkylene arylene radicals having from 8 to 12 carbon atoms and arylene radicals; X and X' are selected from hydrogen or an alkyl radical having from 1 to 4 carbon atoms; and each n is a number from 0 (zero) to 4.

Col. 4, lines 16-38. The Knapp formula contains a broad range of variables and thus encompasses a large number of different diphenols, one of which is bisphenol A, which is shown in Baird's application as having the following structure:



Knapp also discloses that the dicarboxylic acids have the general formula:

HOOCR'' 'n₃COOH wherein R'' ' is a substituted or unsubstituted alkylene radical having from 1 to 12 carbon atoms, arylene radicals or alkylene arylene radicals having from 10 to 12 carbon atoms and n₃ is a number of less than 2.

Col. 5, lines 6-14. Twenty typical dicarboxylic acids are recited, including succinic acid, glutaric acid, and adipic acid, the dicarboxylic acids recited in claim 1.

The examiner rejected claim 1 as obvious on the ground that Knapp specifically discloses as components of his esters the three dicarboxylic acids recited in claim 1 and a generic formula which encompasses bisphenol A. Recognizing that bisphenol A is defined when certain specific variables are chosen, the examiner reasoned that bisphenol A "may be easily derived from the generic formula of the diphenol in [Knapp] and all the motivation the worker of ordinary skill in the art needs to arrive at the particular polyester of the instant claim[] is to follow [that formula]."

The Board upheld the examiner's rejection. It rejected Baird's argument that there was no motivation for one to select bisphenol A from Knapp and summarily concluded that "the fact that [the claimed] binder resin is clearly encompassed by the generic disclosure of Knapp . . . provides ample motivation for the selection of [the claimed composition]." Slip op. at 3. The Board's decision was affirmed on reconsideration.

DISCUSSION

The only issue before us is whether the record supports the Board's conclusion that, in view of the teachings of Knapp, the claimed compounds 2 would have been obvious to one of ordinary skill in the art. We review an obviousness determination by the Board *de novo*, while we review underlying factual findings for clear error. *In re Beattie*, 974 F.2d 1309, 1311, 24 USPQ2d 1040, 1041 (Fed. Cir. 1992).

Baird does not dispute the fact that the generic diphenol formula of Knapp encompasses bisphenol A. Nor does Baird dispute that Knapp specifically discloses the three dicarboxylic acids recited in claim 1. Rather, Baird argues that there is no suggestion in Knapp to select bisphenol A from the vast

number of diphenols covered by the generic formula and that the Board thus erred in concluding that the claimed compounds would have been obvious.

[1] What a reference teaches is a question of fact. *Beattie*, 974 F.2d at 1311, 24 USPQ2d at 1041. The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (rejecting Commissioner's argument that "regardless [] how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it"). *Jones* involved an obviousness rejection of a claim to a specific compound, the 2-(2'-aminoethoxy)ethanol salt of 2-methoxy-3,6-dichlorobenzoic acid (dicamba), as obvious in view of, *inter alia*, a prior art reference disclosing a genus which admittedly encompassed the claimed salt. We reversed the Board's rejection, reasoning that the prior art reference encompassed a "potentially infinite genus" of salts of dicamba and listed several such salts, but that it did not disclose or suggest the claimed salt. *Id.*

In the instant case, the generic diphenol formula disclosed in Knapp contains a large number of variables, and we estimate that it encompasses more than 100 million different diphenols, only one of which is bisphenol A. While the Knapp formula unquestionably encompasses bisphenol A when specific variables are chosen, there is nothing in the disclosure of Knapp suggesting that one should select such variables. Indeed, Knapp appears to teach away from the selection of bisphenol A by focusing on more complex diphenols, including 2,2-bis(4-beta-hydroxyethoxyphenyl) propane, 2,2-bis(4-hydroxypropoxyphenyl) propane, and 2,2-bis(4-hydroxyisopropoxyphenyl)propane. Col. 4, lines 51-64. Knapp teaches that in preferred diphenols, R has 2 to 4 carbon atoms and R' and R'' have 3 to 4 carbon atoms, and in "optimum" diphenols, R is an isopropylidene radical, R' and R'' are selected from the group consisting of propylene and butylene radicals, and n is one. Col. 4, lines 38-47. Knapp further states that the diphenol in the preferred polyester material is 2,2-bis(4-hydroxyisopropoxyphenyl)propane. Col. 5, lines 36-38. Fifteen typical diphenols are recited. None of them, or any of the other preferred phenols recited above, is or suggests bisphenol A.

The Commissioner repeatedly emphasizes that many of the diphenols specifically enumerated in Knapp are derivatives of bisphenol A. He argues that Knapp thus suggests the selection of bisphenol A itself. We disagree, because, according to the specification, the diphenol in the esters of claim 1 can only be bisphenol A, not a bisphenol A derivative. While Knapp may suggest certain complex bisphenol A derivatives, it does not describe or suggest bisphenol A and therefore does not motivate the selection of bisphenol A.

"[A] reference must be considered not only for what it expressly teaches, but also for what it fairly suggests." *In re Burckel*, 592 F.2d 1175, 1179, 201 USPQ 67, 70 (CCPA 1979). Given the vast number of diphenols encompassed by the generic diphenol formula in Knapp, and the fact that the diphenols that Knapp specifically discloses to be "typical," "preferred," and "optimum" are different from and more complex than bisphenol A, we conclude that Knapp does not teach or fairly suggest the selection of bisphenol A. *See In re Belle* 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993) (DNA sequence would not have been obvious in view of prior art reference suggesting a nearly infinite number of possibilities and failing to suggest why among all those possibilities one would seek the claimed sequence). A disclosure of millions of compounds does not render obvious a claim to three compounds, particularly when that disclosure indicates a preference leading away from the claimed compounds.

CONCLUSION

The Board clearly erred in finding that Knapp would have provided the requisite motivation for the selection of bisphenol A in the preparation of the claimed compounds. Accordingly, the decision of the Board affirming the rejection of claim 1 as obvious over Knapp is reversed.

COSTS

No costs. *REVERSED*

Footnotes

Footnote 1. The real party in interest is Lexmark International, Inc.

Footnote 2. Since the toner, the resin, and the polyester compounds appear to be treated in the Board opinion and patent application as synonymous, and the PTO has premised its obviousness rejection on the obviousness of the compounds, we will treat this case accordingly.

- End of Case -

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Version 

FULL TEXT OF CASES (USPQ2D)

All Other Cases

In re Vaeck (CA FC) 20 USPQ2d 1438 (10/21/1991)

In re Vaeck (CA FC) 20 USPQ2d 1438

In re Vaeck

U.S. Court of Appeals Federal Circuit

20 USPQ2d 1438

Decided October 21, 1991

No. 91-1120

Headnotes

PATENTS

1. Patentability/Validity - Obviousness - Combining references (§ 115.0905)

Rejection of claimed subject matter as obvious under 35 USC 103 in view of combination of prior art references requires consideration of whether prior art would have suggested to those of ordinary skill in art that they should make claimed composition or device, or carry out claimed process, and whether prior art would also have revealed that such person would have reasonable expectation of success; both suggestion and reasonable expectation of success must be founded in prior art, not in applicant's disclosure.

2. Patentability/Validity - Obviousness - Relevant prior art - Particular inventions (§ 115.0903.03)

Patent and Trademark Office has failed to establish prima facie obviousness of claims for use of genetic engineering techniques for producing proteins that are toxic to insects such as larvae of mosquitos and black flies, since prior art does not disclose or suggest expression in cyanobacteria of chimeric gene encoding insecticidally active protein, or convey to those of ordinary skill reasonable expectation of success in doing so; expression of antibiotic resistance-conferring genes in cyanobacteria, without more, does not render obvious expression of unrelated genes in cyanobacteria for unrelated purposes.

3. Patentability/Validity - Specification - Enablement (§ 115.1105)

JUDICIAL PRACTICE AND PROCEDURE

Procedure - Judicial review - Standard of review - Patents (§ 410.4607.09)

Specification must, in order to be enabling as required by 35 USC 112, first paragraph, teach person skilled in art to make and use invention without "undue experimentation," which does not preclude some experimentation; enablement is question of law which is reviewed independently on appeal, although such determination is based upon underlying factual findings which are reviewed for clear error.

PATENTS

4. Patentability/Validity - Specification - Enablement (§ 115.1105)

Patent and Trademark Office did not err in rejecting, as non-enabling pursuant to 35 USC 112, first paragraph, claims for use of genetic engineering techniques for producing proteins that are toxic to insects such as larvae of mosquitos and black flies, in view of relatively incomplete understanding of biology of cyanobacteria as of applicants' filing date, as well as limited disclosure by applicants of particular cyanobacterial genera operative in claimed invention, since there is no reasonable correlation between narrow disclosure in applicants' specification and broad scope of protection sought in claims encompassing gene expression in any and all cyanobacteria.

Case History and Disposition:

Page 1439

Appeal from the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences.

Application for patent, serial no. 07/021,405, filed March 4, 1987, by Mark A. Vaeck, Wipa Chungiatupornchai, and Lee McIntosh (hybrid genes incorporating a DNA fragment containing a gene coding for an insecticidal protein, plasmids, transformed cyanobacteria expressing such protein and method for use as a biocontrol agent). From decision rejecting claims 1-48 and 50-52 as unpatentable under 35 USC 103, and rejecting claims 1-48 and 50-51 for lack of enablement, applicants appeal. Affirmed and part and reversed in part; Mayer, J., dissents with opinion.

Attorneys:

Ian C. McLeod, Okemos, Mich., for appellant.

Teddy S. Gron, associate solicitor (Fred E. McKelvey, solicitor and Richard E. Schafer, associate solicitor, with him on brief), for appellee.

Judge:

Before Rich, Archer, and Mayer, circuit judges.

Opinion Text

Opinion By:

Rich, J.

This appeal is from the September 12, 1990 decision of the Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences (Board), affirming the examiner's rejection of claims 1-48 and 50-52 of application Serial No. 07/021,405, filed March 4, 1987, titled "Hybrid Genes Incorporating a DNA Fragment Containing a Gene Coding for an Insecticidal Protein, Plasmids, Transformed Cyanobacteria Expressing Such Protein and Method for Use as a Biocontrol Agent" as unpatentable under 35 USC 103, as well as the rejection of claims 1-48 and 50-51 under 35 USC 112, first paragraph, for lack of enablement. We reverse the § 103 rejection. The § 112 rejection is affirmed in part and reversed in part.

BACKGROUND

A. The Invention

The claimed invention is directed to the use of genetic engineering techniques 1 for production of proteins that are toxic to insects such as larvae of mosquitos and black flies. These swamp-dwelling pests are the source of numerous human health problems, including malaria. It is known that certain species of the naturally-occurring *Bacillus* genus of bacteria produce proteins ("endotoxins") that are toxic to these insects. Prior art methods of combatting the insects involved spreading or spraying crystalline spores of the insecticidal *Bacillus* proteins over swamps. The spores were environmentally unstable, however, and would often sink to the bottom of a swamp before being consumed, thus rendering this method prohibitively expensive. Hence the need for a lower-cost method of producing the insecticidal *Bacillus* proteins in high volume, with application in a more stable vehicle.

As described by appellants, the claimed subject matter meets this need by providing for the production of the insecticidal *Bacillus* proteins within host cyanobacteria. Although both cyanobacteria and bacteria are members of the procaryote 2 kingdom, the

Page 1440

cyanobacteria (which in the past have been referred to as "blue-green algae") are unique among procaryotes in that the cyanobacteria are capable of oxygenic photosynthesis. The cyanobacteria grow on top of swamps where they are consumed by mosquitos and black flies. Thus, when *Bacillus* proteins are produced within transformed 3 cyanobacterial hosts according to the claimed invention, the presence of the insecticide in the food of the targeted insects advantageously guarantees direct uptake by the insects.

More particularly, the subject matter of the application on appeal includes a chimeric (i.e., hybrid) gene comprising (1) a gene derived from a bacterium of the *Bacillus* genus whose product is an insecticidal protein, united with (2) a DNA promoter effective for expressing 4 the *Bacillus* gene in a host cyanobacterium, so as to produce the desired insecticidal protein.

The claims on appeal are 1-48 and 50-52, all claims remaining in the application. Claim 1 reads:

1. A chimeric gene capable of being expressed in Cyanobacteria cells comprising:
 - (a) a DNA fragment comprising a promoter region which is effective for expression of a DNA fragment in a Cyanobacterium; and
 - (b) at least one DNA fragment coding for an insecticidally active protein produced by a *Bacillus* strain, or coding for an insecticidally active truncated form of the above protein or coding for a protein having substantial sequence homology to the active protein,
 the DNA fragments being linked so that the gene is expressed.

Claims 2-15, which depend from claim 1, recite preferred *Bacillus* species, promoters, and selectable markers. 5 Independent claim 16 and claims 17-31 which depend therefrom are directed to a hybrid plasmid vector which includes the chimeric gene of claim 1. Claim 32 recites a bacterial strain. Independent claim 33 and claims 34-48 which depend therefrom recite a cyanobacterium which expresses the chimeric gene of claim 1. Claims 50-51 recite an insecticidal composition. Claim 52 recites a particular plasmid that appellants have deposited.

B. Appellants' Disclosure

In addition to describing the claimed invention in generic terms, appellants' specification discloses two particular species of *Bacillus* (*B. thuringiensis*, *B. sphaericus*) as sources of insecticidal protein; and nine genera of cyanobacteria (*Synechocystis*, *Anacystis*, *Synechococcus*, *Agmenellum*, *Aphanocapsa*, *Gloeocapsa*, *Nostoc*, *Anabaena* and *Ffremyllia*) as useful hosts.

The working examples relevant to the claims on appeal detail the transformation of a single strain of cyanobacteria, i.e., *Synechocystis* 6803. In one example, *Synechocystis* 6803 cells are transformed with a plasmid comprising (1) a gene encoding a particular insecticidal protein ("B.t. 8") from *Bacillus thuringiensis* var. *israelensis*, linked to (2) a particular promoter, the P_L promoter from the bacteriophage Lambda (a virus of *E. coli*). In another example, a different promoter, i.e., the *Synechocystis* 6803 promoter for the rubisco operon, is utilized instead of the Lambda P_L promoter.

C. The Prior Art

A total of eleven prior art references were cited and applied, in various combinations, against the claims on appeal.

The focus of Dzelzkalns, 6 the primary reference cited against all of the rejected claims, is to determine whether chloroplast promoter sequences can function in cyanobacteria. To that end Dzelzkalns discloses the expression in cyanobacteria of a chimeric gene comprising a chloroplast promoter sequence fused to a gene encoding the enzyme chloramphenicol acetyl transferase (CAT). 7 Importantly, Dzelzkalns teaches the use of the CAT gene as a "marker" gene; this use of antibiotic resistance-conferring genes for selection purposes is a common technique in genetic engineering.

Page 1441

Sekar I, 8 Sekar II, 9 and Ganesan 10 collectively disclose expression of genes encoding certain *Bacillus* insecticidal proteins in the bacterial hosts *B. megaterium*, *B. subtilis* and *E. coli*.

Friedberg 11 discloses the transformation of the cyanobacterium *Anacystis nidulans* R2 by a plasmid vector comprising the O_LP_L operator-promoter region and a temperature-sensitive repressor gene of the bacteriophage Lambda. While the cyanobacteria are attractive organisms for the cloning of genes involved in photosynthesis, Friedberg states, problems may still be encountered such as suboptimal expression of the cloned gene, detrimental effects on cell growth of overexpressed, highly hydrophobic proteins, and rapid turnover of some gene products. To address these problems, Friedberg teaches the use of the disclosed Lambda regulatory signals in plasmid vehicles which, it states, have "considerable potential for use as vectors the expression of which can be controlled in *Anacystis*"

Miller 12 compares the initiation specificities *in vitro* of DNA-dependent RNA polymerases 13 purified from two different species of cyanobacteria (*Fremyella diplosiphon* and *Anacystis nidulans*), as well as from *E. coli*.

Nierzwicki-Bauer 14 identifies in the cyanobacterium *Anabaena* 7120 the start site for transcription of the gene encoding *rbc* L, the large subunit of the enzyme ribulose-1, 5-bisphosphate carboxylase. It reports that the nucleotide sequence 14-8 base pairs preceding the transcription start site "resembles a good *Escherichia coli* promoter," but that the sequence 35 base pairs before the start site does not.

Chauvat 15 discloses host-vector systems for gene cloning in the cyanobacterium *Synechocystis* 6803, in which the antibiotic resistance-conferring *neo* gene is utilized as a selectable marker.

Reiss 16 studies expression in *E. coli* of various proteins formed by fusion of certain foreign DNA sequences with the *neo* gene.

Kolowsky 17 discloses chimeric plasmids designed for transformation of the cyanobacterium *Synechococcus* R2, comprising an antibiotic-resistant gene linked to chromosomal DNA from the *Synechococcus* cyanobacterium.

Barnes, United States Patent No. 4,695,455, is directed to the treatment with stabilizing chemical reagents of pesticides produced by expression of heterologous genes (such as those encoding *Bacillus* proteins) in host microbial cells such as *Pseudomonas* bacteria. The host cells are killed by this treatment, but the resulting pesticidal compositions exhibit prolonged toxic activity when exposed to the environment of target pests.

D. The Grounds of Rejection

1. The § 103 Rejections

Claims 1-6, 16-21, 33-38, 47-48 and 52 (which include all independent claims in the application) were rejected as unpatentable under 35 USC 103 based upon Dzelzkalns in view of Sekar I or Sekar II and Ganesan. The examiner stated that Dzelzkalns discloses a chimeric gene capable of being highly expressed in a cyanobacterium, said gene comprising a promoter region effective for expression in a cyanobacterium operably linked to a structural gene encoding CAT. The examiner acknowledged that the chimeric gene and transformed host of Dzelzkalns differ from the claimed invention in that the former's structural gene encodes CAT rather than insecticidally active protein. However, the examiner pointed out, Sekar I, Sekar II, and Ganesan teach genes encoding insecticidally active proteins produced by *Bacillus*, and the advantages of expressing such genes in heterologous 18 hosts to obtain larger quantities of the protein. The examiner contended that it would have been obvious to one of ordinary skill in the art to substitute the *Bacillus* genes taught by Sekar I, Sekar II, and Ganesan for the CAT gene in the vectors of Dzelzkalns in order to obtain high level expression of the *Bacillus* genes in the transformed cyanobacteria. The examiner further contended that it would have been obvious to use cyanobacteria as heterologous hosts for expression of the claimed genes due to the ability of cyanobacteria to serve as transformed hosts for the

Page 1442

expression of heterologous genes. In the absence of evidence to the contrary, the examiner contended, the invention as a whole was prima facie obvious.

Additional rejections were entered against various groups of dependent claims which we need not address here. All additional rejections were made in view of Dzelzkalns in combination with Sekar I, Sekar II, and Ganesan, and further in view of other references discussed in Part C above.

The Board affirmed the § 103 rejections, basically adopting the examiner's Answer as its opinion while adding a few comments. The legal conclusion of obviousness does not require absolute certainty, the Board added, but only a reasonable expectation of success, citing *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). In view of the disclosures of the prior art, the Board concluded, one of ordinary skill in the art would have been motivated by a reasonable expectation of success to make the substitution suggested by the examiner.

2. The § 112 Rejection

The examiner also rejected claims 1-48 and 50-51 under 35 USC 112, first paragraph, on the ground that the disclosure was enabling only for claims limited in accordance with the specification as filed. Citing *Manual of Patent Examining Procedure* (MPEP) provisions 706.03(n) 19 and (z) 20 as support, the examiner took the position that undue experimentation would be required of the art worker to practice the claimed invention, in view of the unpredictability in the art, the breadth of the claims, the limited number of working examples and the limited guidance provided in the specification. With respect to unpredictability, the examiner stated that

he cyanobacteria comprise a large and diverse group of photosynthetic bacteria including large numbers of species in some 150 different genera including *Synechocystis*, *Anacystis*, *Synechococcus*, *Agmenellum*, *Nostoc*, *Anabaena*, etc. The molecular biology of these organisms has only recently become the subject of intensive investigation and this work is limited to a few genera. Therefore the level of unpredictability regarding heterologous gene expression in this large, diverse and relatively poorly studied group of procaryotes is high....

The Board affirmed, noting that "the limited guidance in the specification, considered in light of the relatively high degree of unpredictability in this particular art, would not have enabled one having ordinary skill in the art to practice the broad scope of the claimed invention without undue experimentation. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)."

OPINION

A. Obviousness

We first address whether the PTO erred in rejecting the claims on appeal as prima facie obvious within the meaning of 35 USC 103. Obviousness is a legal question which this court independently reviews, though based upon underlying factual findings which we review under the clearly erroneous standard. *In re Woodruff*, 919 F.2d 1575, 1577, 16 USPQ2d 1934, 1935 (Fed. Cir. 1990).

[1] Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. See *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. *Id.*

[2] We agree with appellants that the PTO has not established the prima facie obviousness of the claimed subject matter. The prior art simply does not disclose or suggest the expression in cyanobacteria of a chimeric gene encoding an insecticidally active protein, or convey to those of ordinary skill a reasonable expectation of success in doing so. More particularly, there is no suggestion in Dzelzkalns, the primary reference cited against all claims, of substituting in the disclosed plasmid a structural gene encoding *Bacillus* insecticidal proteins for the CAT gene utilized for selection purposes. The expression of antibiotic resistance-conferring genes in cyanobacteria, without more, does not render obvious the expression of unrelated genes in cyanobacteria for unrelated purposes.

The PTO argues that the substitution of insecticidal *Bacillus* genes for CAT marker genes in cyanobacteria is suggested by the secondary references Sekar I, Sekar II, and Ganesan, which collectively disclose expression of genes encoding *Bacillus* insecticidal proteins in two species of host *Bacillus* bacteria (*B. megaterium* and *B. subtilis*) as well as in the bacterium *E. coli*. While these references disclose expression of *Bacillus* genes encoding insecticidal proteins in certain transformed bacterial hosts, nowhere do these references disclose or suggest expression of such genes in transformed cyanobacterial hosts.

To remedy this deficiency, the PTO emphasizes similarity between bacteria and cyanobacteria, namely, that these are both procaryotic organisms, and argues that this fact would suggest to those of ordinary skill the use of cyanobacteria as hosts for expression of the claimed chimeric genes. While it is true that bacteria and cyanobacteria are now both classified as procaryotes, that fact alone is not sufficient to motivate the art worker as the PTO contends. As the PTO concedes, cyanobacteria and bacteria are not identical; they are classified as two separate divisions of the kingdom Procaryotae. 21 Moreover, it is only in recent years that the biology of cyanobacteria has been clarified, as evidenced by references in the prior art to "blue-green algae." Such evidence of recent uncertainty regarding the biology of cyanobacteria tends to rebut, rather than support, the PTO's position that one would consider the cyanobacteria effectively interchangeable with bacteria as hosts for expression of the claimed gene.

At oral argument the PTO referred to additional secondary references, not cited against any independent claim (i.e., Friedberg, Miller, and Nierzwicki-Bauer), which it contended disclose certain amino acid sequence homology between bacteria and cyanobacteria. The PTO argued that such homology is a further suggestion to one of ordinary skill to attempt the claimed invention. We disagree. As with the Dzelzkalns, Sekar I, Sekar II, and Ganesan references discussed above, none of these additional references disclose or suggest that cyanobacteria could serve as hosts for expression of genes encoding *Bacillus* insecticidal proteins. In fact, these additional references suggest as much about *differences* between cyanobacteria and bacteria as they do about similarities. For example, Nierzwicki-Bauer reports that a certain nucleotide sequence (i.e., the -10 consensus sequence) in a particular cyanobacterium resembles an *E. coli* promoter, but that another nearby nucleotide sequence (the -35 region) does not. While Miller speaks of certain promoters of the bacteriophage Lambda that are recognized by both cyanobacterial and *E. coli* RNA polymerases, it also discloses that these promoters exhibited differing strengths when exposed to the different polymerases. Differing sensitivities of the respective polymerases to an inhibitor are also disclosed, suggesting differences in the structures of the initiation complexes.

The PTO asks us to agree that the prior art would lead those of ordinary skill to conclude that cyanobacteria are attractive hosts for expression of any and all heterologous genes. Again, we can not. The relevant prior art does indicate that cyanobacteria are attractive hosts for expression of both native and heterologous *genes involved in photosynthesis* (not surprisingly, for the capability of undergoing oxygenic photosynthesis is what makes the cyanobacteria unique among procaryotes). However, these references do not suggest that cyanobacteria would be equally attractive hosts for expression of *unrelated* heterologous genes, such as the claimed genes encoding *Bacillus* insecticidal proteins.

In *O'Farrell*, this court affirmed an obviousness rejection of a claim to a method for

Page 1444

producing a "predetermined protein in a stable form" in a transformed bacterial host. 853 F.2d at 895, 7 USPQ2d at 1674. The cited references included a prior art publication (the Polisky reference) whose three authors included two of the three coinventor-appellants. The main difference between the prior art and the claim at issue was that in Polisky, the heterologous gene was a gene for ribosomal RNA, while the claimed invention substituted a gene coding for a predetermined protein. *Id.* at 901, 7 USPQ2d at 1679. Although, as the appellants therein pointed out, the ribosomal RNA gene is not normally translated into protein, Polisky mentioned preliminary evidence that the transcript of the ribosomal RNA gene was translated into protein, and further predicted that if a gene coding for a protein were to be substituted, extensive translation might result. *Id.* We thus affirmed, explaining that

the prior art explicitly suggested the substitution that is the difference between the claimed invention and the prior art, and presented preliminary evidence suggesting that the [claimed] method could be used to make proteins.

....

... Polisky contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful.

Id. at 901-02, 7 USPQ2d at 1679-80.

In contrast with the situation in *O'Farrell*, the prior art in this case offers no suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art. Moreover, the "reasonable expectation of success" that was present in *O'Farrell* is not present here. Accordingly, we reverse the § 103 rejections.

B. Enablement

[3] The first paragraph of 35 USC 112 requires, *inter alia*, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without "undue experimentation." *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). That *some* experimentation may be required is not fatal; the issue is whether the amount of experimentation required is "undue." *Id.* at 736-37, 8 USPQ2d at 1404. Enablement, like obviousness, is a question of law which we independently review, although based upon underlying factual findings which we review for clear error. *See id.* at 735, 8 USPQ2d at 1402.

In response to the § 112 rejection, appellants assert that their invention is "pioneering," and that this should entitle them to claims of broad scope. Narrower claims would provide no real protection, appellants argue, because the level of skill in this art is so high, art workers could easily avoid the claims. Given the disclosure in their specification, appellants contend that any skilled microbiologist could construct vectors and transform many different cyanobacteria, using a variety of promoters and *Bacillus* DNA, and could easily determine whether or not the active *Bacillus* protein was successfully expressed by the cyanobacteria.

The PTO made no finding on whether the claimed invention is indeed "pioneering," and we need not address the issue here. With the exception of claims 47 and 48, the claims rejected under § 112 are not limited to any particular genus or species of cyanobacteria. The PTO's position is that the cyanobacteria are a diverse and relatively poorly studied group of organisms, comprising some 150 different genera, and that heterologous gene expression in cyanobacteria is "unpredictable." Appellants have not effectively disputed these assertions. Moreover, we note that only one particular species of cyanobacteria is employed in the working examples of appellants' specification, and only nine genera of cyanobacteria are mentioned in the entire document.

[4] Taking into account the relatively incomplete understanding of the biology of cyanobacteria as of appellants' filing date, as well as the limited disclosure by appellants of particular cyanobacterial genera operative in the claimed invention, we are not persuaded that the PTO erred in rejecting claims 1-46 and 50-51 under § 112, first paragraph. There is no reasonable correlation between the narrow disclosure in appellants' specification and the broad scope of protection sought in the claims encompassing gene expression in any and all cyanobacteria. *See In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (the first paragraph of § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification).

Page 1445

22 Accordingly, we affirm the § 112 rejection as to those claims.

In so doing we do *not* imply that patent applicants in art areas currently denominated as "unpredictable" must never be allowed generic claims encompassing more than the particular species disclosed in their specification. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Angstadt*, 537 F.2d 498, 502-03, 190 USPQ 214, 218 (CCPA 1976). However, there must be sufficient disclosure, either through illustrative examples or terminology, 23 to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility. Where, as here, a claimed genus represents a diverse and relatively poorly understood group of microorganisms, the required level of disclosure will be greater than, for example, the disclosure of an invention involving a "predictable" factor such as a mechanical or electrical element. *See Fisher*, 427 F.2d at 839, 166 USPQ at 24. In this case, we agree with the PTO that appellants' limited disclosure does not enable one of ordinary skill to make and use the invention as now recited in claims 1-46 and 50-51 without undue experimentation.

Remaining dependent claim 47 recites a cyanobacterium which expresses the chimeric gene of claim 1, wherein the cyanobacterium is selected from among the genera *Anacystis* and *Synechocystis*. Claim 48, which depend from claim 47, is limited to the cyanobacterium *Synechocystis* 6803. The PTO did not separately address these claims, nor indicate why they should be treated in the same manner as the claims encompassing all types of cyanobacteria. Although these claims are not limited to expression of genes encoding particular *Bacillus* proteins, we note what appears to be an extensive understanding in the prior art of the numerous *Bacillus* proteins having toxicity to various insects. The rejection of claims 47-48 under § 112 will not be sustained.

CONCLUSION

The rejection of claims 1-48 and 50-52 under 35 USC 103 is *reversed*. The rejection of claims 1-46 and 50-51 under 35 USC 112, first paragraph, is *affirmed* and the rejection of claims 47 and 48 thereunder is *reversed*.

AFFIRMED-IN-PART, REVERSED-IN-PART

Footnotes

Footnote 1. Basic vocabulary and techniques for gene cloning and expression have been described in *In re O'Farrell*, 853 F.2d 894, 895-99, 7 USPQ2d 1673, 1674-77 (Fed. Cir. 1988), and are not repeated here.

Footnote 2. All living cells can be classified into one of two broad groups, procaryotes and eucaryotes. The procaryotes comprise organisms formed of cells that do not have a distinct nucleus; their DNA floats throughout the cellular cytoplasm. In contrast, the cells of eucaryotic organisms such as man, other animals, plants, protozoa, algae and yeast have a distinct nucleus wherein their DNA resides.

Footnote 3. "Transformed" cyanobacteria are those that have successfully taken up the foreign *Bacillus* DNA such that the DNA information has become a permanent part of the host cyanobacteria, to be replicated as new cyanobacteria are generated.

Footnote 4. "Expression" of a gene refers to the production of the protein which the gene encodes; more specifically, it is the process of transferring information from a gene (which consists of DNA) via messenger RNA to ribosomes where a specific protein is made.

Footnote 5. In the context of the claimed invention, "selectable markers" or "marker genes" refer to antibiotic-resistance conferring DNA fragments, attached to the gene being expressed, which facilitate the selection of successfully transformed cyanobacteria.

Footnote 6. *Nucleic Acids Res.* 8917 (1984).

Footnote 7. Chloramphenicol is an antibiotic; CAT is an enzyme which destroys chloramphenicol and thus imparts resistance thereto.

Footnote 8. *Biochem. and Biophys. Res. Comm.* 748 (1986).

Footnote 9. *Gene* 151 (1985).

Footnote 10. *Mol. Gen. Genet.* 181 (1983).

Footnote 11. *Mol. Gen. Genet.* 505 (1986).

Footnote 12. *J. Bacteriology* 246 (1979).

Footnote 13. RNA polymerase, the enzyme responsible for making RNA from DNA, binds at specific nucleotide sequences (promoters) in front of genes in DNA, and then moves through the gene making an RNA molecule that includes the information contained in the gene. Initiation specificity is the ability of the RNA polymerase to initiate this process specifically at a site(s) on the DNA template.

Footnote 14. *Proc. Natl. Acad. Sci. USA* 5961 (1984).

Footnote 15. *Mol. Gen. Genet.* 185 (1986).

Footnote 16. *Gene* 211 (1984).

Footnote 17. *Gene* 289 (1984).

Footnote 18. Denotes different species or organism.

Footnote 19. MPEP 706.03(n), "Correspondence of Claim and Disclosure," provides in part:

In chemical cases, a claim may be so broad as to not be supported by [the] disclosure, in which case it is rejected as unwarranted by the disclosure....

Footnote 20. MPEP 796.03(z), "Undue Breadth," provides in part:

n applications directed to intentions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Sol*, 1938 C.D. 723; 497 O.G. 546. This is because in arts such as chemistry it is not obvious from the disclosure of one species, what other species will work. *In re Dreshfield*, 1940 C.D. 351; 518 O.G. 255 gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." ...

Footnote 21. *Stedman's Medical Dictionary* 1139 (24th ed. 1982) (definition of "Procaryotae"). Procaryotic organisms are commonly classified according to the following taxonomic hierarchy: Kingdom; Division; Class; Order; Family; Genus; Species. 3 *Bergey's Manual of Systematic Bacteriology* 1601 (1989).

Footnote 22. The enablement rejection in this case was not based upon a post-filing date state of the art, as in *In re Hogan*, 559 F.2d 595, 605-07, 194 USPQ 527, 536-38 (CCPA 1977). See also *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 USPQ2d 1461, 1464 (Fed. Cir. 1989) (citing *Hogan*); *Hormone Research Found., Inc. v. Genentech, Inc.*, 904 F.2d 1558, 1568-69, 15 USPQ2d 1039, 1047-48 (Fed. Cir. 1990) (directing district court, on remand, to consider effect of *Hogan* and *United States Steel* on the enablement analysis of *Fisher*), cert. dismissed, — U.S. —, 111 S. Ct. 1434 (1991). We therefore do not consider the effect of *Hogan* and its progeny on *Fisher*'s analysis of when an inventor should be allowed to "dominate the future patentable inventions of others." *Fisher*, 427 F.2d at 839, 166 USPQ at 24.

Footnote 23. The first paragraph of § 112 requires nothing more than *objective* enablement. *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is irrelevant. *Id.*

Dissenting Opinion Text

Dissent By:

Mayer, J., dissenting.

An appeal is not a second opportunity to try a case or prosecute a patent application, and we should not allow parties to "undertake to retry the entire case on appeal." *Perini America, Inc. v. Paper Converting Machine Co.*, 832 F.2d 581, 584, 4 USPQ2d 1621, 1624 (Fed. Cir. 1987); *Eaton Corp. v. Appliance Valves Corp.*, 790 F.2d 874, 877, 229 USPQ 668, 671 (Fed. Cir. 1986). But that is precisely what the court has permitted here. The PTO conducted a thorough examination of the prior art surrounding this patent application and concluded the claims would have been obvious. The board's decision based on the examiner's answer which comprehensively explains the rejection is persuasive and shows how the evidence supports the legal conclusion that the claims would have been obvious. Yet, the court ignores all this and conducts its own examination, if you will, as though the examiner and board did not exist. Even if thought this opinion were more persuasive than the board's, I could not join it because it misperceives the role of the court.

The scope and content of the prior art, the similarity between the prior art and the claims, the level of ordinary skill in the art, and what the prior art teaches are all questions of fact. *Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966); *Jurgens v. McKasy*, 927 F.2d 1552, 1560, 18 USPQ2d 1031, 1037 (Fed. Cir. 1991). And "[w]here there are two permissible views of

Page 1446

the evidence, the factfinder's choice between them cannot be clearly erroneous." *Anderson v. City of Bessemer City*, 470 U.S. 564, 574 (1985). The mere denomination of obviousness as a question of law does not give the court license to decide the factual matters afresh and ignore the requirement that they be respected unless clearly erroneous. *In re Woodruff*, 919 F.2d 1575, 1577, 16 USPQ2d 1934, 1935 (Fed. Cir. 1990); *In re Kulling*, 897 F.2d 1147, 1149, 14 USPQ2d 1056, 1057 (Fed. Cir. 1990). There may be more than one way to look at the prior art, but on this record we are bound by the PTO's interpretation of the evidence because it is not clearly erroneous and its conclusion is unassailable. I would affirm on that basis.

- End of Case -

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